

## MATERNAL OUTCOMES OF PREGNANCY-RELATED ACUTE KIDNEY INJURY

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### ABSTRACT

**Objective:** To determine the frequency of Pregnancy-related acute kidney injury in the Pakistani population and its effect on maternal health.

**Study Design:** Cross-sectional study.

**Place and Duration of the Study:** Department of Nephrology and Obstetrics and Gynecology, Combined Military Hospital Kharian, from Jan 2018 to Dec 2020.

**Methodology:** All pregnant women with normal renal functions at the time of enrolment in the study and no previous history of any kidney disease or renal procedure in the recent past (at least 3 months) before conception were included in our study at Combined Military Hospital Kharian. All participants had serum creatinine tested at enrolment and were inquired specifically about any history of renal disease or any renal procedure in the recent past (at least 3 months old).

**Results:** Mean maternal age in the study was  $29 \pm 7.67$  years however it ranged from 16-41 years. Around a quarter of acute kidney injury cases occurred in the first and second trimesters combined, with 26 (12%) and 24 (11%) cases in the first and second trimesters, respectively. Thirty percent of acute kidney injury cases were diagnosed in the third trimester. A substantial number 58 (27%) of cases developed azotemia which persisted beyond three months and developed chronic kidney disease of various stages. Regarding maternal outcomes, 166 (77%) mothers recovered completely. However, 43 (20%) patients had some degree of azotemia, a few cases required permanent renal replacement therapy.

**Conclusion:** Acute kidney injury is a common problem in our community leading to suboptimal maternal outcomes. Overall prognosis is relatively better but there is a definitive association with the development of chronic kidney disease and even permanent dialysis dependency.

**Keywords:** Acute kidney injury, Hemolytic uraemic syndrome thrombotic thrombocytopenic purpura (TTP), Renal failure in pregnancy.

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### INTRODUCTION

Acute kidney injury represents a challenging clinical problem, especially when it occurs at some stage during pregnancy for both obstetricians and nephrologists. Pregnancy-related acute kidney injury has major implications for both maternal and fetal health and pregnancy outcomes.<sup>1</sup> Despite recent advances in obstetrics and nephrology care overall pregnancy-related kidney injury remains uncharted territory. Causes that are responsible for AKI in the general public can cause AKI during pregnancy, but Pr-AKI may have causes specifically related to pregnancy. The true incidence of AKI is not known exactly because of lack of consensus on the definition of AKI in pregnancy as hyperfiltration during pregnancy leads to subnormal values of urea and creatinine so what appears normal in ordinary population may represent the extremely compromised renal function and is likely to be missed

by treating physicians.<sup>2</sup> While the frequency of Pr-AKI requiring dialysis in developed countries is low (1 in 2000 cases), in underdeveloped countries incidence of up to 10-20% has been reported which is a major health dilemma.<sup>3</sup>

There is a dire need to explore this issue especially in underdeveloped world countries and get some valuable data and insight into this clinical conundrum. The information obtained will enable government agencies and health professionals to better plan and treat this potentially fatal health issue.

### METHODOLOGY

This was a cross-sectional study was carried from January 2018 to December 2020. Previously a Chinese study by Diankun *et al.* has reported, "AKI occurred in 393 (3.6%) and 402 (3.7%) of the pregnant women, respectively, giving rise to an overall AKI incidence of 7.3%. While hospital coding would have identified less than 5% of AKI episodes." Moreover, he also mentioned that, "incidence of AKI during pregnancy in developing countries, such as India, and Pakistan ranged

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from 0.02-11.5%". Ali *et al.* mentioned obstetric related AKI incidence of 9-11% in 2007. The sample size was calculated using the Raosoft sample size calculator. With a 5% margin of error and 95% confidence interval estimated size was around 259 cases due to time and financial constraints we swapped to non-probability consecutive sampling.

**Inclusion Criteria:** All the ladies reporting for the antenatal visit were examined and evaluated for evidence of AKI and those who fulfilled our criteria of AKI were included in the study.

**Exclusion Criteria:** Patients suffering from chronic kidney disease, hypertension, diabetes mellitus, renal transplantation, liver failure, heart failure or any malignancy were excluded. Those patients who had undergone some urological procedure in the preceding three months were also excluded.

AKI was diagnosed and staged by Kidney Disease Improving Global Outcomes (KDIGO) criteria. Informed consent was taken. Approval of the Ethical committee was taken Ref: no. 1100/adm/2. The primary outcomes were the Frequency proportion of Pr-AKI. Secondary outcomes were in-hospital and post-discharge maternal outcomes including mortality, the requirement for dialysis, renal recovery, and length of stay in hospital. Full clinical examination was done by consultants or registrars. A blood sample was collected in a 10cc sterile syringe and sent to the hospital laboratory by hospital staff. Complete blood count, blood urea, serum creatinine, ESR, CRP and urine analysis) were done. Renal biopsy was performed on patients who had no clearly defined cause for their renal insufficiency for more than 3 weeks.

Data was entered in Statistical Package for the social sciences (SPSS) version 23. Descriptive statistics were calculated as means, standard deviation and percentages for Age, maternal outcome, serum creatinine, survival, and long-term morbidities. The significance of the difference in means was calculated using paired sample t-test, the *p*-value of  $\leq 0.05$  was labelled as significant.

## RESULTS

A total of 216 population developed AKI during our study time period and were included in the study. The mean age of the mother with Pr-AKI was  $29 \pm 7.67$  years. We divided mothers into three main age groups. Pr-AKI was not very common in young mothers as 43 (20%) mothers with Pr-AKI were in the age group up to 20 years. Similar figures 43 (23%) were observed in

the age group (21-30) years. An alarming rise was noted in mothers belonging to the 3<sup>rd</sup> group (>30 years) as 124 (57.4 %) belonged to this age group. Therefore, most of the Pr-AKI cases occurred in mothers of advanced age. Regarding maternal outcomes, the overall prognosis was good as 115 (53%) recovered completely, evidenced by complete clinical and laboratory parameters returning to normal. At the same time, 28 (27%) cases developed azotemia which persisted beyond three months, following the initial AKI event. They were labelled as chronic kidney disease (CKD). A substantial number of cases 9 (13.4%) developed severe enough azotemia to require dialysis. 24 (11%) mothers belonged to Upper Class in comparison to 72 (33%) from the middle class shown in Table-I.

**Table-I: Demographics and outcomes of the study population.**

Study Variables	n (%)
<b>Age</b>	
<20 years	43 (19.9)
21-30 years	49 (22.7)
>30 years	124 (57.4)
<b>Outcome</b>	
Complete Recovery	115 (53.2%)
Chronic Kidney disease	58 (26.9%)
Dialysis Dependent	29 (13.4 %)
Death	14 (6.5%)
<b>Socio Economic Class</b>	
Upper Class	24 (11.1%)
Middle Class	72 (33.3%)
Lower Class	120 (55.6%)

Most of the Pr-AKI was observed in lowerclass 120 (55%), majority of women with AKI belonged to rural areas 121 (56%) which were more than Urban areas 96 (44.4%). We divided timings of occurrence of AKI into four-time frames i.e. The three trimesters and the post-partum period. Around a quarter of acute kidney, injury cases occurred in the first and second trimesters combined, with 26 (12%) and 24 (11%) cases of acute kidney injury occurring in the first and second trimester, respectively. Thirty percent of acute kidney injury cases were diagnosed in the third trimester. A substantial number 58 (27%) of cases developed azotemia which persisted beyond three months and developed chronic kidney disease of various stages. Regarding maternal outcomes, 166 (77%) mothers recovered completely. However, 43 (20%) patients had some degree of azotemia, a few cases required permanent renal replacement therapy. Regarding causes of AKI, sepsis and postpartum haemorrhage were the commonest causes of AKI accounting for >60% of cases. For further details of other causes are shown in the Figure.

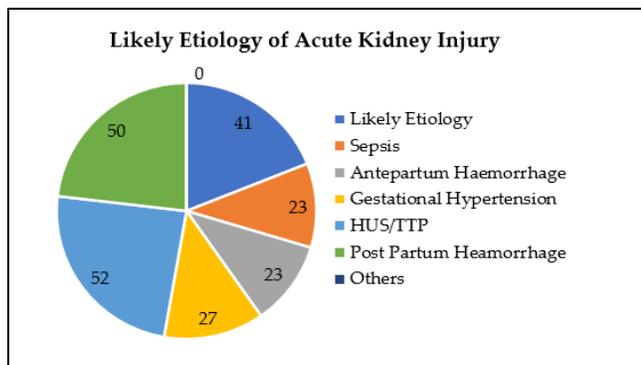


Figure: Various aetiologies of acute kidney injury in pregnancy.

The mean creatinine varied widely between the three trimesters. It reduced to the lowest value of  $186 \pm 92.11$   $\mu\text{mol/l}$  in the second trimester after starting at the mean value of  $203 \pm 249$ ,<sup>5</sup>  $\mu\text{mol/l}$  in the first trimester. There was no statistically significant difference between both trimesters  $p=0.236$  the highest mean creatinine was found in the third trimester at  $310 \pm 283.35$   $\mu\text{mol/l}$ , there was a statistically significant difference between the second and third-trimester  $p<0.001$  and first and third-trimester  $p<0.001$  shown in Table-II.

Table-II: Comparison of serum creatinine and trimester.

Parameters	Trimester		p-value
Serum creatinine (umol/l)	1st Trimester	2nd Trimester	0.236
	203 ± 249	186 ± 92.106	
	2nd Trimester	3rd Trimester	<0.001
	186 ± 92.106	310 ± 283	
	3rd Trimester	1st Trimester	<0.001
	310 ± 283	203 ± 249	

## DISCUSSION

Obstetrics related AKI is a huge health-related problem faced by both developing and underdeveloped countries.<sup>6</sup> However recently a decline has been noted in the incidence of Pr-AKI in developed countries contrary to underdeveloped countries. A study carried out in Italy showed that the frequency of obstetrics related AKI has reduced from a total incidence of 43% to 0.5% of total reported cases of AKI and 1/3000 to 1/18,000 of total pregnancies in three decades.<sup>7</sup>

The above-mentioned trend is causing increasing problems for developing countries as their health resources are limited and renal failure is a resource-draining disease with high morbidity and mortality. Even rich and technologically advanced countries like Australia are struggling to fight this disease.<sup>8</sup> There are a few local studies to give an insight into this complex issue. A recent local study was carried out by Haroon et al. They found that the mean age was 29.90 years. Out of 111 cases, 10 (9%) developed AKI in the 1st tri-

mester, 12 (10.8%) in the 2nd trimester, 13 (11.7%) cases in the 3rd trimester, and major bulk of the cases of AKI occurred in the post-partum period= 76 (68.4%). The causes of Pr-AKI were multiple and varied in different patients. The frequencies of complications leading to AKI were observed individually.<sup>9</sup> Similarly maximum cases of AKI occurred in the post-partum period. However, their percentage (68%) was well more than ours at 47%. In addition, they studied the causes of AKI individually, but it was out of scope in our study. Their study did not show any association of AKI with advanced maternal age but in our study frequency of AKI was highest in the age group (30 and above) mothers as (57%) belonged to this age group.

Rizwan *et al*, at Karachi, described meaning age 26 (29 years in our study). They related AKI to gravidity also which was not the case in our study. Regarding maternal outcome, they quoted 68% of a mother with AKI underwent dialysis which is remarkably high compared to ours 29 (13%). In their study three-month follow-up showed complete resolution of AKI in 14 (34.2%) patients, partial resolution in 7 (17%), end-stage renal disease in 10 (24.4%), and death in 10 (24.4%) patients.<sup>10</sup> In comparison, our population 115 (53%) recovered completely, 58 (27%) developed CKD and 29 (13%) became permanently dialysis-dependent. Death frequency was exceptionally low in our study at 14 (7%) compared to them. So clearly our maternal outcomes were better than their population and the difference may have been due to diverse cultural backgrounds, economic classes, and varying health resource access facilities.<sup>10</sup>

To add to the confusion there is wide variation in maternal outcome figures in numerous studies carried out in different counties and various setups within the same country. For example, Elfeky *et al* had far better maternal outcomes compared to ours and other studies in South Asia. They reported complete recovery in 87% of the patients, which is more than all the studies quoted above. Similarly, only 4% of mothers ended up in dialysis and only 1.4% died during the study period. These differences might have been due to distinct cultural and medical facilities in Egypt, but their study population was only 70 patients which are relatively insignificant compared to our study >200 patients. Furthermore, we followed up patients for three months after the event of AKI and assigned them to various outcomes. Their follow-up time was 6 months which may have given more time for kidneys to recover completely and hence remarkably high rates of comp-

lete recovery in their population.<sup>1</sup> Another study from Malawi by Cook was a landmark study on the same issue. They studied an exceptionally large population of 322 patients with Pr-AKI and the incidence of AKI was 8%. Surprisingly enough in contradiction to most of the world literature, no women with AKI died or required dialysis and complete renal recovery occurred in 22 (84.6%) cases. These results were most promising in all the studies compared so far,<sup>11</sup> Many of their results were not in keeping with most of the published literature as their results were better than most of the published literature.<sup>5,12-18</sup>

Therefore, in nutshell, our findings were in keeping with most of the local studies and literature in under-developed countries. However, outcome figures varied widely in different studies which may be the result of different study designs, population sizes and variable definitions of AKI.<sup>19-24</sup> All literature of the world is unanimous on the fact that high morbidity and mortality is associated with Pr-AKI and this issue needs early recognition and prompt management.

## CONCLUSION

Acute kidney injury is a common problem complicating pregnancies in district Gujrat of Pakistan. However, the overall prognosis is good as most of the mothers developing Aki during pregnancy regained normal renal function. Despite all this, a limited proportion of patients ended up in potentially disabling and life-threatening complications of chronic kidney disease.

**Conflict of Interest:** None.

## Authors' Contribution

MIK: Direct contribution, SNK: Direct contribution, AI: Intellectual contribution, KK: Intellectual contribution, UY: Intellectual contribution.

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